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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,168	02/04/2004	Gregory E. Gonye	BC1042 USDIV1	5566

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EXAMINER	
SHIBUYA, MARK LANCE	
ART UNIT	**PAPER NUMBER**
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,168	GONYE ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya, Ph.D.	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-6 and 9-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/4/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 3-6 and 9-13 are pending.

Election/Restrictions

2. Applicant's election without traverse of the species of host that is prokaryotes in the Paper, filed 10/18/2006, is acknowledged.

Priority

3. This application, filed 2/4/2004, states that it is a divisional of 09/832,419, filed 4/11/2001, now US Patent No. 6,716,582, issued 4/11/2001, which claims benefit of 60/197,348, filed 4/14/2000.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 3-6 and 9-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3, and its dependent claims, recites the limitation "an organism" and "a host organism" in lines 5 and 7, respectively. There is uncertain antecedent basis for these limitations in the claim.

Claim 3, and its dependent claims, recites the limitation "an organism" and "a host organism" in lines 5 and 7, respectively. There is uncertain antecedent basis for these limitations in the claim.

Claim 5, and its dependent claims, recites the limitation "a promoterless reporter gene or reporter gene". There is uncertain antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 3, 4, 9,12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Ashby et al., U.S. Patent No. 5,569,588 (IDS entered 2/4/2004).

The claims are drawn to a method for generating a genome-registered collection of reporter gene fusions comprising the steps of: (a) generating a set of gene fusions comprising: 1) a reporter gene or reporter gene complex operably linked to 2) a genomic fragment from an organism of which at least 15% of the genomic nucleotide sequence is known; (b) introducing in vitro the reporter gene fusions from step (a) into a host organism; (c) registering the reporter gene fusions on the basis of sequence homology to the genomic sequence of the organism; (d) repeating (a), (b), and/or (c)

until reporter gene fusions have been made to at least 15% of the known genomic nucleotide sequence of said organism; and variations thereof.

Ashby et al. throughout the patent and especially at the abstract, teach a method of detecting reporter gene product signals from each of a plurality of different, separately isolated cells of a target organism, wherein each of said cells contains a recombinant construct comprising a reporter gene operatively linked to a different endogenous transcriptional regulatory element (e.g. promoter) of said target organism such that said transcriptional regulatory element regulates the expression of said reporter gene, wherein said plurality of cells comprises an ensemble of the transcriptional regulatory elements of said organism sufficient to model the transcriptional responsiveness of said organism to a drug, contacting each said cell with a candidate drug, detecting reporter gene product signals from each of said cells before and after contacting each of said cells with said candidate drug to obtain a drug response profile, wherein said drug response profile provides an estimate of the physiological specificity or biological interactions of said candidate drug (column 1).

Ashby et al., at col. 6, line 50-col. 7, line 22, teach genome reporter matrices comprising a plurality of different separately isolated cells of a target organism under one or more a variety of physical conditions, such as temperature and pH, medium and osmolarity. Ashby et al., teach fusions as arrayed onto microtiter plates. Ashby et al., state:

> Each of the cells contains a recombinant construct comprising a reporter gene operatively linked to a different endogenous transcriptional regulatory element of said target organism such that said transcriptional regulatory element regulates the expression of said reporter gene. A

> sufficient number of different recombinant cells are included to provide an ensemble of transcriptional regulatory elements of said organism sufficient to model the transcriptional responsiveness of said organism to a drug. In a preferred embodiment, the matrix is substantially comprehensive for the selected regulatory elements, e.g. essentially all of the gene promoters of the targeted organism are included. Other cis-acting or trans-acting transcription regulatory regions of the targeted organism can also be evaluated.

Ashby et al., at col. 6, lines 60-65.

This reference teaches an ensemble of reporting cells for use in the methods that comprises as comprehensive a collection of transcription regulatory genetic elements as is conveniently available for the targeted organism so as to most accurately model the systemic transcriptional response. Suitable ensembles generally comprise thousands of individually reporting elements; preferred ensembles are substantially comprehensive, i.e. provide a transcriptional response diversity comparable to that of the target organism. Generally, a substantially comprehensive ensemble requires transcription regulatory elements from at least a majority of the organism's genes, and preferably includes those of all or nearly all of the genes. We term such a substantially comprehensive ensemble a genome reporter matrix. It is frequently convenient to use an ensemble or genome reporter matrix derived from a lower eukaryote or common animal model to obtain preliminary information on drug specificity in higher eukaryotes, such as humans (column 2).

Ashby et al teach an application of the genome reporter matrix in antibiotic and antifungal discovery. They teach that the genome reporter matrix offers a new tool to solve the problem of finding pharmaceutical targets in fungi that are specific to the fungus. Specifically, all molecules that fail to elicit any response in the Saccharomyces

reporter are collected into a set, which by definition must be either inactive biologically or have a very high specificity. A reporter library is created from the targeted pathogen such as Cryptococcus, Candida, Aspergillus, Pneumocystis etc., i.e., fungi, (as in claim 9). All molecules from the set that do not affect Saccharomyces are tested on the pathogen, and any molecule that elicits an altered response profile in the pathogen in principle identifies a target that is pathogen-specific (column 5). This teaching reads on having assembled two genome-wide scale collections (because the reference teaches that these, which they call genome reporter matrix, are used in this particular method), perturbing each collection (both the Saccharomyces reporter collection and an additional fungus reporter collection) by adding the presence of a chemical (the elected species) to each collection. The response is measured from both reporter collections and analyzed to identify patterns of similarities and differences, as shown by the reference teaching that any molecule that elicits an altered response profile (which is a pattern of similarities when not altered, and a pattern of differences when altered) in the pathogen in principle identifies a target that is pathogen. Determination of altered response profiles between the two reporter collections determines (differences and similarities of) gene function between the two organisms. Thus, the method steps of the claimed invention are taught by the cited reference.

This reference also teaches one embodiment of the method in which the reporter gene used is lacZ, (as in claim 12), and that a wide variety of reporters known in the art can be used, such as green fluorescent protein, lacZ, etc (column 7). The nucleotide

sequence of Saccharomyces is over 50% known, (as in claim 13), because the whole genomic sequence is known in the art.

Furthermore, Ashby, at col. 6, lines 3-28), contemplate methods comprising a genome reporter matrix for organisms that are bacterial, as in claim 9).

The genome reporter matrix taught by Ashby et al reads on genome-registered collections because it is a set of strains containing reporter gene fusions to at least a majority of all known or predicted promoter regions. Although Ashby et al do not specifically indicate that the genome reporter matrix has been mapped by homology to the nucleic acid sequence of the genome of the organism, Ashby et al teach that the ensemble of strains is comprehensive (corresponding to a majority of the organism's genes, each of which is different from the others in the ensemble). "Mapping by homology" is merely acquiring homology information concerning the clones in the collection, which does not alter the structure of the collection, and thus a genome-registered collection has no structural difference from a collection that is not genome-registered. Accordingly, the genome reporter matrix taught by Ashby et al has the same structure as a genome-registered collection as claimed. And, because the same method steps, using the same products, are taught by the cited reference, the teachings of Ashby et al anticipate the claimed invention.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 3-6 and 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Ashby et al.**, U.S. Patent No. 5,569,588, (IDS entered 2/4/2004), and in view of **Larossa et al.**, U.S. Patent No. 6,025,131, (IDS entered 2/4/2004).

The claims are drawn to a method for generating a genome-registered collection of reporter gene fusions, as in claim 3, further comprising generating random nucleic acid fragments and operably linking the random nucleic fragments to a promoterless reporter gene, as in claims 5 and 6; and further comprising an organism that is an enteric bacterium, including *Escherichia* and *Salmonella*, as in claims 9-11.

Ashby et al., U.S. Patent No. 5,569,588, is relied upon as above in the rejection under 35 USC 102(b).

Ashby et al., does not disclose methods comprising generating random nucleic acid fragments and operably linking the random nucleic fragments to a promoterless reporter gene; and further comprising an organism that is an enteric bacterium, including *Escherichia* and *Salmonella*.

Larossa et al., U.S. Patent No. 6,025,131, throughout the patent and abstract, teach methods for identifying promoters, including e.g., at col. 11, line 20-col. 12, line 16, col. 14, lines 11-35, col. 16, line 45-col. 17, line 30, creating gene fusions where a regulatory region, responsive to some cellular stress, is fused to a luminescent reporter gene complex, wherein random fragments of genomic DNA are prepared by restriction digest or primer directed methods, (as in claim 5 and 6). Larossa et al., at col. 18, lines 26-38, disclose sequencing inserted DNA, to identify the inserted DNA in a plasmid. Larossa et al., at e.g., col. 10, lines 1-27, teach organisms that are enteric bacteria, (as in claim 9), including *Escherichia* and *Salmonella*, as in claim 11. Larossa et al., at col. 10, lines 34-55, teach reporter gene complexes that include *luxCDABE*, as in claim 12.

It would have been *prima facie* obvious, at the time the invention was made, for one of ordinary skill in the art to have made and used a method for generating a genome-registered collection of reporter gene fusions, further comprising generating random nucleic acid fragments and operably linking the random nucleic fragments to a promoterless reporter gene; and further comprising an organism that is an enteric bacterium, including *Escherichia* and *Salmonella*, as in claims 9-11.

One of ordinary skill in the art would have been motivated to make and use methods for generating a set of gene fusing comprising random fragments from DNA of an organism because it is desirable to discover promoters and other gene regulatory regions, as taught by Larossa at col. 3, lines 14-33, col. 3, lines 3-62. One of ordinary skill in the art would have been motivated to use enteric bacteria, because Larossa et al., at col. 12, line 40-col. 13, line 10, teach that *E. coli* is a desirable bacterial strain to test effects of a chemical because various mutations of *E. coli* are know to permit permeation and accumulation of chemicals of interest into the cell.

One of ordinary skill in the art would have had a reasonable expectation of success in using methods of methods for generating a set of gene fusing comprising random fragments from DNA of an organism and further comprising an organism that is an enteric bacterium, including *Escherichia* and *Salmonella*, because Larossa et al., at col. 3, lines 1-24, teach that using reporter genes to discover promoters are long known in the art, as is the use of enteric bacteria, such as *Escherichia*.

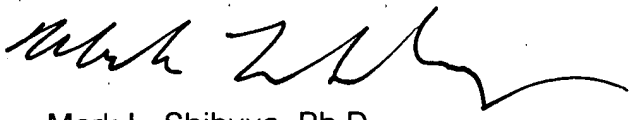
Conclusion

10. Claims 3-6 and 9-13 are rejected.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Shibuya, whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. James Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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